AMENDED COPY

Protocol 1023-020
Final, May 25, 1999
Amended, August 6, 1999

PROTOCOL 1023-020 SYNOPSIS

TITLE A Phase 2, Randomized, Multicenter, 26-Week Study to Assess the Efficacy and Safety of CI-1023 Delivered Through Minimally Invasive Surgery Versus Maximum Medical Treatment in Patients With Severe Angina, Advanced Coronary Artery Disease, and No Options for Revascularization

INDICATION Severe angina due to advanced atherosclerotic Coronary Artery Disease (CAD)

OBJECTIVES To assess the efficacy and safety of a dose of CI-1023 delivered through Minimally Invasive Surgery (MIS) in treating patients with advanced CAD and to compare them against patients who received maximum medical treatment

PATIENT POPULATION Patients with advanced CAD and angina (Canadian Cardiovascular Society [CCS] Angina Class III to IV, excluding prolonged [unstable] angina at rest) who are incompletely controlled with maximum medical therapy and are not candidates for Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG)

STUDY DESIGN A randomized, multicenter, 26-week, Phase 2 trial

TREATMENT CI-1023 ($Ad_{GV}VEGF_{121.10}$) 4×10^{10} particle units (pu) administered directly into the myocardium in 30 divided injections (in 100 µL each) at 1.5 to 2.0 cm intervals covering the left ventricle (no CI-1023 injections or MIS in the maximum medical treatment group)

PRIMARY EFFICACY PARAMETER(S) Change from baseline compared to maximum medical treatment in the time to onset of at least 1 mm additional ST-segment depression on exercise ECG, or termination of ETT in the absence of at least 1 mm additional ST-segment depression, at Week 12

SECONDARY EFFICACY PARAMETERS Change from baseline compared to maximum medical treatment in other ETT parameters at Week 12 and 26 (total exercise duration, time to onset of Level 2 angina, and peak [maximum] rate pressure product [heart rate × systolic blood pressure], time to onset of at lest 1 mm additional ST-segment depression at Week 26); and change from baseline in Summed Stress Score (SSS) at Week 12 and 26 (The SSS is a semiquantitative perfusion variable determined by ^{99m}Tc-sestamibi SPECT), global wall motion scores (rest and ETT stress) and Summed Reversibility (difference) Score (SDS) determined by ^{99m}Tc-sestamibi SPECT